

Research: 10 packages, each containing approximately 500 milligrams.

(b) *Tests and methods of assay*—(1) *Potency*. Use either of the following methods; however, the results obtained from the hydroxylamine colorimetric assay shall be conclusive.

(i) *Microbiological agar diffusion assay*. Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed sample in sufficient 1 percent potassium phosphate buffer, pH 6.0 (solution 1), to give a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with solution 1 to the reference concentration of 20 micrograms of cefadroxil per milliliter (estimated).

(ii) *Hydroxylamine colorimetric assay for cefadroxil*. Proceed as directed in § 442.40(b)(1)(ii), except prepare the working standard and sample solutions and calculate the potency of the sample as follows:

(A) *Preparation of working standard solutions*. Dissolve and dilute an accurately weighed portion of the cefadroxil working standard in sufficient distilled water to obtain a stock solution of convenient concentration. Further dilute an aliquot of this solution with distilled water to a concentration of 1 milligram of cefadroxil per milliliter.

(B) *Preparation of sample solutions*. Dissolve an accurately weighed portion of the sample in sufficient distilled water to obtain a stock solution of convenient concentration. Further dilute an aliquot of this solution with distilled water to a concentration of 1 milligram of cefadroxil per milliliter (estimated).

(C) *Calculations*. Calculate the potency of the sample in micrograms per milligram as follows:

$$\frac{\text{Micrograms of cefadroxil}}{\text{per milligram}} = \frac{A_U \times P_a \times 100}{A_s \times W_U \times (100 - m)}$$

where:

$A_U$ =Absorbance of sample solution;

$A_s$ =Absorbance of working standard solution;

$P_a$ =Potency of working standard solution in micrograms per milliliter;

$W_U$ =Milligrams of sample per milliliter of sample solution; and

$m$ =Percent moisture content of the sample.

(2) [Reserved]

(3) *Moisture*. Proceed as directed in § 436.201 of this chapter.

(4) *pH*. Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 50 milligrams per milliliter.

(5) *Absorptivity*. Determine the absorbance of the sample and standard solutions in the following manner: Dissolve accurately weighed portions of approximately 50 milligrams each of the sample and standard in 250 milliliters of distilled water. Transfer a 10-milliliter aliquot to a 100-milliliter volumetric flask and dilute to volume with distilled water. Using a suitable spectrophotometer and distilled water as the blank, determine the absorbance of each solution at 264 nanometers. Determine the percent absorptivity of the sample relative to the absorptivity of the standard using the following calculations:

Percent relative absorptivity = [Absorbance of sample X milligrams standard X potency of standard in micrograms per milligram X 10]/[Absorbance of standard X milligrams sample X (100- $m$ )]

where:

$m$  = Percent moisture in the samples.

(6) *Identity*. Using the sample and working standard solutions prepared as described in paragraph (b)(5) of this section and a suitable spectrophotometer, record the ultraviolet spectrum from 220 to 340 nanometers. The spectrum of the sample compares qualitatively with that of the cefadroxil working standard.

(7) *Crystallinity*. Proceed as directed in § 436.203(a) of this chapter.

[59 FR 8857, Feb. 24, 1994]

#### § 442.8a Sterile cefamandole nafate.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Sterile cefamandole nafate is the sodium salt of 7-*D*-mandelamido-3-[[[1-methyl-1*H*-tetrazol-5-yl)thio]methyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]-oct-2-ene-2-carboxylate formate (ester). It is so purified and dried that:

(i) Its potency is not less than 810 micrograms and not more than 1,000

micrograms of cefamandole per milligram on an anhydrous basis.

- (ii) It is sterile.
- (iii) It is nonpyrogenic.
- (iv) [Reserved]
- (v) Its moisture content is not more than 2.0 percent.
- (vi) Its pH in an aqueous solution containing 100 milligrams per milliliter is not less than 3.5 and not more than 7.0.

(vii) It passes the identity test.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, sterility, pyrogens, moisture, pH, and identity.

(ii) Samples required:

(a) For all tests except sterility: 10 packages, each containing approximately 500 milligrams.

(b) For sterility testing: 20 packages, each containing equal portions of approximately 250 milligrams.

(b) *Tests and methods of assay*—(1) *Potency.* Use any of the following methods; however, the results obtained from the hydroxylamine colorimetric assay shall be conclusive.

(i) *Hydroxylamine colorimetric assay.* Proceed as directed in § 442.40(b)(1)(ii) of this chapter, except use the cefamandole working standard.

(ii) *Polarographic assay.* Proceed as directed in § 436.324 of this chapter.

(iii) *Microbiological agar diffusion assay.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed sample in sufficient 0.1M potassium phosphate buffer, pH 8.0 (solution 3), to obtain a concentration of 1 milligram of cefamandole per milliliter (estimated). Hydrolyze this solution in a 37° C constant temperature water bath for 60 minutes. Further dilute a portion of the hydrolyzed solution with 1 percent potassium phosphate buffer, pH 6.0 (solution 1), to the reference concentration of 2.0 micrograms of cefamandole per milliliter (estimated).

(2) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the meth-

od described in paragraph (e)(1) of that section.

(3) *Pyrogens.* Proceed as directed in § 436.32(b) of this chapter, using a solution containing 50 milligrams of cefamandole per milliliter.

(4) [Reserved]

(5) *Moisture.* Proceed as directed in § 436.201 of this chapter.

(6) *pH.* Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 100 milligrams per milliliter.

(7) *Identity.* Proceed as directed in § 436.211 of this chapter, using the mineral oil mull prepared as described in paragraph (b)(2) of that section.

[47 FR 32708, June 1, 1982, as amended at 50 FR 19919, May 13, 1985]

#### § 442.9a Sterile cefamandole sodium.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Sterile cefamandole sodium is 5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[(hydroxyphenylacetyl)amino]-3-[[[(1-methyl-1H-tetrazol-5-yl)thio]methyl]-8-oxo-, monosodium salt [6R-[6 $\alpha$ , 7 $\beta$ (R\*)]]-. It is so purified and dried that:

(i) Its cefamandole content is not less than 860 micrograms and not more than 1,000 micrograms of cefamandole per milligram on an anhydrous basis.

(ii) It is sterile.

(iii) It is nonpyrogenic.

(iv) [Reserved]

(v) Its moisture content is not more than 3.0 percent.

(vi) Its pH in an aqueous solution containing 100 milligrams per milliliter is not less than 3.5 and not more than 7.0.

(vii) It passes the identity test.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for cefamandole content, sterility, pyrogens, moisture, pH, and identity.

(ii) Samples required:

(a) For all tests except sterility: 10 packages, each containing approximately 500 milligrams.